

**REMARKS:**

Reconsideration of the present application is respectfully requested for the reasons that follow.

Claim Amendments

Claims 1 and 32-35 have been amended to incorporate some of the limitations of the immediately prior version of claim 7 and all of the limitations of the immediately prior version of claim 8, which at least provide written description support for these amendments. No new matter is added. Consequently, claim 7 has been amended to remove this incorporated subject matter, thus requiring the conversion of claim 7 into an independent claim, and claim 8 has been canceled.

New claim 36 has been added. Written description support for this amendment can be found at least in the immediate prior version of claims 1 and 7. No new matter is added.

Claim Rejections under 35 USC § 102(b)

The Examiner has rejected claims 1, 3-7, 9 and 32-35 under 35 USC § 102(b) as being anticipated by Crameri (*Gene*, vol. 137, 1993, pp. 69-75). Crameri is directed to a cloning and expression system allowing the display of cDNAs on the surface of a filamentous phage which utilizes the interaction between leucine zipper proteins. The Examiner argues that Crameri teaches a first fusion protein PIII comprising a Jun-Leucine-Zipper domain and a pelB signal sequence, as well as a second fusion protein derived from a cDNA from a cDNA library, comprising a Fos-Leucine-Zipper domain and a pelB signal sequence. The Examiner argues

that a mixture of these two fusion proteins anticipates the subject matter of independent claims 1 and 32-35. Applicants traverse.

Applicants note that the Examiner further argues that the subject matter of the rejected claims is not considered novel over Crameri because limitations regarding the folding state are considered to be functional features of a process, but not limiting features of the product. A specific structure providing for different folding requirements is allegedly not specified in the claims. Applicants disagree with the Examiner's interpretation of the claims. However, solely in the interest of expediting prosecution, independent claims 1 and 32-35 have been amended to incorporate the limitations of previous claim 8. Since claim 8 is not subject to the anticipation rejection based on Crameri, this amendment to the independent claims renders the rejection moot as to those claims, as well as the claims which depend from them. Accordingly, this rejection should be withdrawn.

#### Claim Rejections under 35 USC § 103(a)

The Examiner has rejected claims 1, 3-9 and 32-35 under 35 USC § 103(a) as being obvious over Crameri (*Gene*, vol. 137, 1993, pp. 69-75) in view of Weiner (US Pat. No. 6,335,178) and further in view of Wu (*Arch. Microbiol.*, vol. 173, 2000, pp. 319-324). Crameri is discussed above. Weiner is directed to compositions and methods for secretion of functional proteins in a soluble form in host cells. Wu is directed to the membrane targeting and translocation of periplasmic and membrane-bound bacterial hydrogenases. The Examiner has also rejected claims 1, 3-9 and 32-35 under 35 USC § 103(a) as being obvious over Crameri (*Gene*, vol. 137, 1993, pp. 69-75) in view of Georgiou (US Pat. No. 7,419,783). Crameri is

discussed above. Georgiou is directed to leader peptides which direct export of heterologous proteins from the bacterial cytoplasm.

The Examiner argues that Crameri is the closest prior art to the subject matter, as Crameri discloses a Jun-Leucine-Zipper domain and a Fos-Leucine-Zipper domain, respectively, and a pelB signal sequence, which leads to the transport in an unfolded state into the periplasm. The Examiner also argues, in part, that the subject matter of claim 8, which specifies that the translocation sequence of the second fusion protein is a Tat or  $\Delta$ -ph dependent sequence, is considered obvious over Crameri in view of Weiner or Georgiou, because Weiner and Georgiou each teach a Tat dependent translocation sequence, which transports proteins through the cytoplasmic membrane in a folded state. Therefore, the Examiner argues that it would have been obvious to one of ordinary skill in the art to combine the Tat translocation sequence with the system of Crameri. In particular, because of the advantages taught by Weiner with respect to the Tat translocation pathway, it would have been obvious for the skilled person to replace one of the pelB translocation sequences with a Tat translocation sequence. Applicants traverse.

Applicants disagree with the Examiner's interpretation of the claims. However, solely in the interest of expediting prosecution, independent claims 1 and 32-35 have been amended to incorporate some of the limitations of the immediately prior version of claim 7. Applicants reiterate the arguments presented in the response to the non-final Office Action filed February 24, 2011. Further, Applicants note that even with the assumption that Weiner teaches advantages of using the Tat translocation pathway, the skilled person would not combine the

teachings of Crameri and Weiner to arrive at the presently claimed subject matter, since he would not replace just one of the translocation sequences of Crameri. Rather, the skilled person would replace both sequences, as he would not have a reason to use the advantages taught by Weiner only for one of the proteins. None of the documents, considered alone or in combination, suggests a fusion protein consisting of two proteins with different translocation sequences, as is presently claimed.

In response to the Applicants' previous arguments with respect to the advantages of the claimed fusion protein, the Examiner alleges that these arguments relate to the use of the fusion protein and the manner of its production process, but not to the fusion protein itself. Further, the system according to the claims is allegedly not an *in vivo* system and Applicants' arguments against the objection based on Choi are not admissible, as one cannot show non-obviousness by attacking a single document if the objection is based on several documents. With respect to Choi, the Examiner is of the opinion that Applicants hold that this document teaches away from the invention. However, the examples and preferred embodiments can allegedly not teach away from a broader disclosure.

Regarding the previous arguments based on the advantages and the production process of the claimed fusion protein, Applicants note that an assessment of the obviousness of the claimed product cannot be made without considering its production process and its use. If only the product itself is considered, the skilled person, without a specific use of the product in mind, could have no motivation at all to invent said product, since it would only be a random

and arbitrary combination of features without a purpose. Therefore, the arguments in response to the previous Office Action should be fully considered by the Examiner.

Further, with respect to the *in vivo/ in vitro* debate, Applicants note that claim 1 undoubtedly discloses an *in vivo* system implicitly, since the features of a translocation in a specific state through the cytoplasmic membrane can only occur in a cell-expression-system. Applicants emphasize that Choi does not disclose the binding of two proteins in an *in vivo* system and further note that this argument is in reply to one of the Examiner's arguments, which she supports with Choi. Applicants' argument is not directed at Choi itself, but at a combination of this document with Crameri and Weiner. Therefore, the objection to this argument is not relevant.

In response to the argument that examples and preferred embodiments cannot teach away from a broader teaching, Applicants' note that this argument has not been raised. Rather, Applicants' argument merely relates to the fact that the skilled person would not have considered Choi due to the difference in the system and that the teaching of this document cannot be applied in the assessment of the claimed subject matter. A teach-away has never been affirmed.

In view of the foregoing amendments and arguments, the obviousness rejection as to independent claims 1 and 32-35, and to their dependent claims, should be withdrawn.

In view of the foregoing, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the pending claims are requested. The Director is authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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